REMARKS

In the Office Action mailed July 25, 2003:

Claims 48 and 49 were indicated to be allowable. Claim 11 was objected to as being dependent upon a rejected base claim but was indicated to be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 54 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

Claims 2 and 51 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims were indicated to be duplicates.

Claims 1-8, 10, 12, 27, 31, 51-53, 55, and 56 were rejected under 35 U.S.C. 102(b) as anticipated by Lin et al..(U.S. Patent 5,591,139).

Claims 1-8, 10, 12, 25-27, 31, 32, 34, 36-37, 50-53, 55 and 56 were rejected under 35 U.S.C. 102(e) as anticipated by Frazier et al..(WO 01/93930).

Claims 9, 13-15, 18 and 20-24 were rejected under 35 U.S.C. 103(a) as unpatentable over Lin et al. in view of Say et al.

Claims 9 and 13-15 were rejected under 35 U.S.C. 103(a) as unpatentable over Frazier et al. in view of Say et al.

Claims 16 and 17 were rejected under 35 U.S.C. 103(a) as unpatentable over Lin et al. in view of Say et al, as applied to claims 9,13-15, 18, and 20-24, further in view of Meade et al.

Claims 16 and 17 were also rejected under 35 U.S.C. 103(a) as unpatentable over Frazier et al. in view of Say et al, as applied to claims 9,13-15, 18, and 20-24, further in view of Meade et al.

Claim 19 was rejected under 35 U.S.C. 103(a) as unpatentable over Lin et al. in view of Say et al, as applied to claims 9,13-15, 18, and 20-24, further in view of Kim et al.

Claim 25 was rejected under 35 U.S.C. 103(a) as unpatentable over Lin et al. in view of Smart et al. (US 5,801,057).

Claims 34 and 36 were rejected under 35 U.S.C. 103(a) as unpatentable over Lin et al. in view of Kim et al.

Claim 54 was rejected under 35 U.S.C. 103(a) as unpatentable over Lin et al., or Frazier et al.

Claim 54 has been cancelled.

Claims 57, 58 and 59 have been added. Claim 57 is supported by the disclosure at page 11, line 15 of the specification that the probe may be thinned in the Z direction. Claim 58 is supported by the disclosure at page 5, lines 7 and 9 and page 19, line 23 that the silicon wafer has a single-crystal structure. Claim 59 is supported by the disclosure on page 12 and especially page 12, line 6.

With respect to the rejection of claims 2 and 51 under 35 U.S.C. 112, second paragraph, as duplicates, claim 51 has been amended to recite that the microprobe portion tapers smoothly in width along at least a portion of the X length dimension. This amendment is also supported by the specification at page 12 and especially at page 12, line 6. As a result of this amendment, claim 51 cannot be deemed a duplicate of claim 2.

Applicants' invention is a microprobe device made in an elongated silicon substrate that terminates in a sharp point at the penetration end and has at least one integrated biosensor. The device may be tapered in the microprobe portion to improve stress distribution during penetration.

In the Office Action mailed July 25, 2003, claims 1-8,10, 12. 27. 31. 37, 51-53, 55, and 56 were rejected under 35 U.S.C. 102(b) as being anticipated by Lin et al. (US 5,591,139).

In contrast to applicants' silicon needle, the microneedle described in Lin et al.'s U.S. Patent 5,591,139 is a complicated affair. While Lin et al. also uses a silicon layer 46 (e.g., Fig. 1A), that is where the similarity stops. As shown in Fig. 2A and throughout the cross-sections shown in Fig. 3, a heavily-doped region 52 of boron is formed in the upper surface of the silicon wafer to a depth of 12 μm. The boron-doped region is used as an etch stop but at a cost because the heavily-doped boron region has significantly greater levels of internal stress than undoped single crystal silicon. The cross-hatching in Fig. 2A illustrates the boron-doped region and Col. 4, lines 56-59 describe this region as follows: "Boron-doped region 52 defines tip region 84 (FIG. 2A), extends along the needle shaft and defines the perimeter of interface region 11, as best shown in FIG. 2A." Elsewhere, Lin et al. explicitly state that "there is no single crystal silicon at the tip region 86, so that the tip is sharper and smaller than the portion of the shaft including single-crystal silicon" (Col. 4, lines 29-32); and they also explain that "tip region 86 of shaft 14 does not contain any single-crystal silicon due to the corner-etching behavior of EDP [ethyleneidamine pyrocatacol]." (Col. 7, lines 43-44).

Following formation of the boron-doped region, a thin (1 μm) silicon nitride 72 structure is then formed as shown in Figs. 3D through 3G on the upper surface of the silicon layer 46. This structure covers a layer 66 of phosphosilicate glass (PSG) and a layer 68 of low temperature oxide (LTO). Following formation of the silicon nitride structure, the PSG layer 66 and the LTO layer 68 are removed from the interior of the structure by etching in hydrofluoric acid (Col. 6, lines 32-34). What is left is a hollow silicon nitride shell that extends along the shaft of the microneedle. This shell functions as a needle bore that is used as a conduit for fluids (Col. 6, lines 46-52).

The subject matter of the Lin et al. patent is described in the paper, "Silicon Processed Microneedles" that was presented at the 7th International Conference on Solid State Sensors and Actuators in Yokohama, Japan, June 7-10, 1993. A copy is enclosed for the Examiner's convenience. This paper provides greater detail of the tip structure. Figure 2(b) provides a clearly labeled cross-sectional view of the microneedle that is similar to Figure 2B in U.S. P. 5,591,139. Figure 6 of "Silicon Processed Microneedles" is a scanning electron micrograph of the tip end of the microneedle, clearly showing the end of the boron-doped silicon spine, and the upper two silicon nitride layers forming the tip and the fluid channel.

As is evident in Figure 6, the boron-doped silicon terminates before the tip, leaving a silicon-nitride layer that defines the tip. The absence of any silicon in the tip is also confirmed by a statement nine lines up from the bottom of the left-hand column of text on page 238: "As is evident in Fig. 2(b), no single-crystal silicon is left at the tip region of the microneedle owing to the corner-etching behavior of EDP." (Citation omitted).

Applicants' invention is not anticipated by Lin et al. As described in the specification and as set forth in the claims, applicants' microprobe device comprises a single piece of silicon.

In contrast, Lin et al.'s needle is complex, consisting of a thin silicon nitride shell supported on a silicon spine. At the penetration end of the needle shaft in the region near the tip, the spine consists of heavily boron-doped silicon only 12 micrometers thick. There is no undoped single-crystal silicon in this region, and the actual tip of Lin et al.'s needle consists of silicon nitride film.

By using a single piece of silicon, applicants are able to provide a much stronger microprobe device and one that can be fabricated much more easily with attendant reductions in assembly time and cost. Applicants avoid altogether the use of the relatively fragile silicon

nitride conduit structure of Lin et al. and the elaborate processing steps that are required to form the silicon nitride casing and then etch away the PSG and LTO layers contained therein. Further, applicants avoid the need to form the boron-doped region and the weaknesses this creates in the resulting structure.

The Office Action also rejects claims 1-8, 10, 12, 25-27, 31, 32, 34, 36-37, 50-53, 55 and 58 under 35 U.S.C. 102(b) as being anticipated by Frazier et al..(WO 01/93930)

Frazier et al., describe a hollow microneedle which can be used either to deliver or extract fluid samples. The shaft of the microneedle has parallel sides with a pointed tip and, optionally, a flange to provide structural support and control penetration depth. The microneedle has a series of openings at its tip and at the top of its shaft for fluid intake/outlet , and one or more biosensors and/or actuators located within the shaft. At page 8, lines 7-14, Frazier et al., states that the microneedle can be fabricated by micromachining techniques from a long list of materials including silicon.

Frazier et al. describe only one method of microneedle fabrication at (page 13, line 9 page 15, line 5). Here, the microneedle is formed by electroplating the needle components on a planar support structure, namely a doped, silicon-nitride-coated single-crystal silicon wafer. Palladurm is described as the preferred material. The wafer acts as a support for the fabrication of the microneedle but does not form any portion of the microneedle itself; rather, the microneedle base, sides, and top are formed of material deposited in sequence on the support. The needles can then be removed from the support. The fabrication method as described in detail uses electrodeposition of the needle base, sides and top using photoresist to define the lumen of the needle. The method is suitable for needles made from electroconductive materials such as metals, which have been the focus of Frazier et al.'s work (page 8, lines 11-14). However since silicon is a semiconductor, not a metal, it is not understood how this electrodeposition method could be used to form a silicon needle. Moreover, even if the fabrication method is somehow modified to use silicon, it is not seen how the resultant needles could be described as formed in a silicon substrate as required in the claims. Further, the flange, which is equivalent to the body of applicant's biosensor microprobe, is not integral to Frazier's device but is attached separately. Frazier et al. also do not disclose electrodes for electrochemical biosensor readout, instead describing a bioluminescence biosensor. Frazier et al. therefore do not anticipate applicant's biosensor microprobe.

With respect to the rejection of dependent claims 9, 13-25, 34 and 36 under 35 U.S.C. 103(a) as obvious over Lin et al., in view of various other references, the other references do not make up for the failure of Lin et al. to disclose the use of a single crystal silicon substrate as claimed by applicants.

Likewise, with respect to the rejection of dependent claims 9, and 13-17 under 35 U.S.C. 103(a) as obvious over Frazier et al., in view of Say et al., and or Say et al., in view of Meade et al., Say et al., and Meade et al., do not disclose the use of a single crystal silicon substrate as claimed by applicant.

In view of the foregoing, applicants believe that all of the claims are now in condition for allowance and respectfully request the Examiner to pass the subject application to issue. If for any reason the Examiner believes any of the claims are not in condition for allowance, he is encouraged to phone the undersigned at (650) 849-7777 so that any remaining issues may be resolved.

Aside for the fees for Petition to Extend Time and for the additional claims, no additional fee is believed due for filing this response. However, if a fee is due, please charge such fee to Morgan, Lewis & Bockius LLP's Deposit Account No. 50-0310.

Respectfully submitted,

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Francis E Morris 24,615

Francis E. Morris (Reg. No.)
MORGAN, LEWIS & BOCKIUS LLP
3300 Hillview Avenue
Palo Alto, CA 94304
(650) 849-7777